I. The Amendments

Support for the amendments that do not add new matter to the noted claims is found in the specification at page 23, lines 25-29, and on page 25, beginning at line 1 continuing to page 26, line 2. The amendments were done to put the claims in condition for allowance and to promote administrative efficiency. The amendments do not require a new search or raise new rejections because they are responsive to issues already raised by the Examiner. Applicants respectfully request entry of the amendments.

II. Drawings

Responsive to form PTO-948, formal drawings are enclosed (eight (8) sheets of five (5) figures. As such, the objection for correction of informalities should be withdrawn.

III. Specification

An abstract on page 131 is enclosed in response to the Examiner's request.

IV. Priority

The Examiner has argued that the subject matter in part b) and part c) of independent claim 33 and the claims dependent thereon are not entitled to the priority date of the provisional application, Serial Number 60/018,175, filed May 23, 1996. Applicants direct the Examiner's attention to page 6, lines 3-14, of the provisional application. In the noted paragraph, the attributes of a synthetic antigen presenting cell (APC) of the present invention are described. In particular, cells, cell fragments, and other solid supports including metals, plastics, porous materials, microbeads, microtiter plates, red blood cells and liposomes are described for use as a synthetic APC. The specification then describes at lines 11-13 that "MHC class II/accessory molecules, having at least their extracellular portions, are operably linked to the supports." Parts b)

and c) of claim 33 recite these elements. The phrase in part c) "capable of loading a selected peptide" is supported in the provisional application at page 5, lines 18-23. The phrase in part c) "such that the extracellular portions of the MHC class II heterodimer and accessory molecule are present on the matrix in sufficient numbers for activating $CD4^+$ T cells when a peptide is loaded onto the extracellular portion of the heterodimer" is supported in the provisional application at page 5, lines 23-29.

Applicants thus contend that claim 33, parts b) and c), and the claims dependent thereon are entitled to claim priority to the provisional application. Applicants request reconsideration of the priority determination of claim 33.

V. Oath/Declaration

Replacement Combined Declarations and Power of Attorney documents for five (5) inventors on four (4) documents of 2 pages each are enclosed. As such, the objection to the defective oaths of record should be withdrawn.

VI. Rejection under 35 U.S.C. §112, First Paragraph

Claims 33, 35-36, 39-43, 45-47, 50-52 and 56-57 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner contends that the description of the present invention lacks the requisite structural and functional features of a broad genus of a synthetic antigen presenting matrix that would meet the recited limitations of antigen presentation, with the exception of insect cells, and the accessory molecules B7.1, B7.2, ICAM-1, ICAM-2, ICAM-3, FASL, CD70 and LFA. The Examiner further argues that the present case is analogous to the requirements established in *Regents of California v. Eli Lilly & Co.*, 119F3d 1559, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), where a description of a genus

of cDNAs was determined as valid by "means of a recitation of a representative number of cDNAs, defined by a nucleotide sequence, falling within the scope of the genus, or of a recitation of the structural features common to the genus, which features constitute a substantial portion of the genus." The court actually held that the adequate description of claimed DNA requires a precise definition of the DNA sequence itself - not merely a recitation of its function or a reference to a potential method for isolating it (119 F.3d at 1566-67, 43 USPQ2d at 1406). In Enzo Biochem, the court clarified Eli Lilly in that the court did not hold that all functional descriptions of genetic material fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure. See *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002).

Applicants argue that the Examiner has misapplied Eli Lilly to the present invention especially in view of a more recent decision by the Federal Circuit addressing the written description holding in Eli Lilly and Enzo Biochem. In *Amgen Inc. v Hoechst Marion Roussel, Inc and Transkaryotic Therapies, Inc.*, 2003 U.S. App. LEXIS 118, decided January 6, 2003, the court held that both Eli Lilly and Enzo Biochem were "inapposite to this case because the claim terms at issue here are not new or unknown biological material that ordinarily skilled artisans would easily miscomprehend." The claims in Amgen's patents referred to mammalian and vertebrate cell types that could be used to express recombinant human EPO. The court found that the words "mammalian" and "vertebrate" conveyed distinguishing information that was readily understood by one of ordinary skill in the art.

The same argument is applicable to the claim terms of the present invention. Here the claim terms of a support, a MHC class II heterodimer, and an accessory molecule are well known to one of ordinary skill in the art of antigen presentation as evidenced by the art of record and the state of the art at the time the invention was made. Moreover, the scope of the claim terms are supported by exemplary description

in the specification including specific examples of preferred embodiments. Supports, including cells, are described at page 40, beginning at line 14, continuing to page 49, line 30, and again at page 78, beginning at line 18, continuing to page 81, line 22. MHC class II genes and encoded heterodimers are described at page 18, beginning at line 19, continuing to page 21, line 2, and again at page 66, beginning at line 18, continuing to page 70, line 28. Accessory genes and the encoded proteins are described 21, beginning at line 4, continuing to page 24, line 2, and again at page 72, beginning at line 14, continuing to page 78, line 16. Thus, the Applicants have clearly conveyed, with reasonable clarity to those of ordinary skill in the art, that as of the filing date, they were in possession of the claimed invention.

For the above reasons, Applicants submit that the rejections for lack of written description have been overcome to the pending claims to a synthetic antigen presenting matrix composition. As such, Applicants respectfully request that the rejections be withdrawn and the claims pass on to allowance.

VII. Double Patenting

Claims 33, 35-36, 41-43, 44-47, 50-52 and 56-57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 8 of U.S. Patent No. 6,355,479.

Upon notification of allowable subject matter, Applicants will submit a Terminal Disclaimer as requested by the Examiner.

VIII. Rejection under 35 U.S.C. §102(e)

Claims 33, 35-36, 41-42, 44-47, 50-52 and 56-57 are rejected under 35 U.S.C. §102(e) as being unpatentable over MacKay et al. (U.S. Patent No. 5,648,219). This rejection is respectfully traversed.

The Examiner argues that MacKay '219 anticipates the present invention as it teaches all the elements of the claim 33. The cited reference teaches an activated dendritic cell transfected with MHC class II, called a JAWS II cell, that when activated expresses the transfected MHC class II heterodimer along with various other cell surface antigens in varying amounts. In MacKay, all the expressed cell surface antigens, with the exception of the MHC class II heterodimer, are naturally occurring in the JAWS II cell.

The present invention contemplates a synthetic antigen presenting matrix that comprises the extracellular portions of a MHC class II heterodimer and an accessory molecule, each operably attached to a support, where both the heterodimer and accessory molecule are not normally present on the support, that broadly includes both cellular and non-cellular embodiments. With a cellular support and particularly essential with all non-cellular supports that are encompassed by the presently pending claims to a composition of a synthetic antigen presenting cell matrix, all the molecules are recombinant molecules expressed in accordance with the teachings of the specification on page 45, lines 1-33, continuing to page 46, line 4, and on page 49, lines 7-18. The extracellular domains of the MHC class II heterodimer and any accessory molecule are not endogenous or naturally present in the support, but rather are affixed to it by a number of different anchoring mechanisms. Applicants have included the word "recombinant" in now amended claim 33 to more clearly define the nature of the antigen presenting molecules that are useful in the context of a matrix that broadly comprises cellular as well as non-cellular supports. The cited reference does not teach cellular or non-cellular antigen presentation systems in which all the antigen presentation components are recombinant molecules.

Therefore, in view of the foregoing, Applicants contend that the rejection for anticipation of the rejected claims is negated. Applicants, thus, respectfully request that the rejection for anticipation be withdrawn and the claims pass on to allowance.

IX. Summary

Applicants believe that a complete response is provided in the foregoing amendments and remarks to each issue and grounds for rejection and objection raised by the Examiner. Applicants submit that patentable subject matter exists with regard to the pending claims and therefore respectfully request favorable action and entry of the presents Amendments and Response. The application is now believed to be in proper condition for allowance and early notification of allowance is earnestly solicited. The Examiner is invited to telephone the undersigned if it would be deemed helpful to advance the application.

Respectfully submitted,

1/15/03
Date

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APPENDIX I

IN THE CLAIMS

Please enter the amendments to claim 33 below.

33. (Amended) A synthetic antigen presenting matrix for activating $CD4^+$ T cells comprising:

a) a support;

b) an extracellular portion of a recombinant MHC class II heterodimer operably linked to the support and capable of loading a selected peptide; and

c) an extracellular portion of at least one recombinant accessory molecule operably linked to the support such that the extracellular portions of the MHC class II heterodimer and accessory molecule are present on the matrix in sufficient numbers for activating $CD4^+$ T cells when a peptide is loaded onto the extracellular portion of the heterodimer.

ABSTRACT

The present invention relates to synthetic antigen-presenting matrices, their methods of making and their methods of use. One such matrix is cells that have been transfected to produce MHC antigen-presenting molecules with one or more accessory molecules. The matrices are used to activate naive $CD4^+$ T cells as well as shift the ongoing activation state into a preferred differentiated population of either Th1 or Th2 cells.